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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,123	10/03/2003	Bernd Klinksiek	Bayer 10261-WCG	2253

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EXAMINER	
MAEWALL, SNIGDHA	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
07/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,123	KLINKSIEK ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-36 and 40-45* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 37-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-36 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of Applicants arguments/remarks, amended claims and IDS filed on 04/24/08 is acknowledged.

Claims 16, 26 and 40 have been amended. New claims 41-45 have been added. Claims 1-15 and 37-39 are withdrawn due to restriction requirements being drawn to non elected invention. Claims **16-36 and 40-45** are under prosecution.

The rejections made under 35 USC 112.1 and 35 USC 112.2 have been withdrawn in view of applicants arguments.

The objection to the specification is withdrawn in view of applicant's submission of priority statement in the specification filed on 04/23/08.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 16-36 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Westesen et al. (US Patent No. 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 200, 16, 402-407).

Westesen et al. discloses an invention relating to the area of administration forms and delivery systems for drugs, vaccines and other bioactive agents. The reference also describes the process of preparing micron and submicron particles of bioactive agents. The process as depicted describes that a solid lipid or bioactive agent or a mixture of solid lipids is melted, stabilizers are added either to the lipid or bioactive agent and to the aqueous phase only depending on their physicochemical characteristics. Stabilizers may also be added or exchanged after homogenization. Drugs or bioactive agents can be melted together with lipid. The aqueous phase is heated to the temperature of the melt before mixing and may contain for example, stabilizers, isotonicity agents, buffering substances, and /or preservatives. The molten compounds are emulsified in an aqueous phase by high pressure homogenization (abstract, column 11 and steps 1-8). Drugs or bioactive agents particularly suitable are listed in column 10, lines 30-60). Ibuprofen and vitamins are also enlisted on the same column. Further in step 8 in column 11, lines 50-55, it is disclosed that the dispersion medium can be reduced by standard techniques such as freeze drying and the lyophilized powder can also be processed into other pharmaceutical formulations such as tablets etc. The bioactive drugs can be dissolved or crystalline or amorphous or a mixture of these crystallographic states. Role of surfactant is described in example 19 on column 24. Various isotonicity agents such as glycerol or xylitol and sucrose, glucose are disclosed

on column 10, lines 10-15. The suspensions and lyophilizates can be used for peroral, buccal, pulmonary etc. depending o n the particle size (see column 14, lines 40-45). The reference further teaches the importance of smaller particle size during drug delivery process (see column 2, lines 10-25). The reference teaches that the drug carrier systems in the micrometer size range are represented as microspheres which are encapsulated (column 3, lines 30-35).

Wetesen et al. do not disclose adding compressible fluid in the supercritical state under pressure to the suspension.

Timothy et al. teaches a method for particle size reduction based on rapid expansion from supercritical fluids, especially CO2. Timothy et al. teaches that the pharmacokinetic properties of both oral and injectable formulations are dependent on the particle size. Small particles are often needed in order to maximize surface are, improve bioavailability and for dissolution requirements. Use of surfactant such as tween 80 is described on page 403 for aiding in the stabilization of drug particles.) also see page 405, second paragraph). Micronization of various drugs were assessed at various temperatures and pressures as depicted on page 404 under the heading "results and discussion." Timothy et al. further disclose that the goal was to produce aqueous suspensions of water insoluble drugs by the RESAS of CO2 solutions(page 402, last paragraph).

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to utilize the compressible fluid in the supercritical state under pressure supercritical fluid such as CO2 as disclosed by Timothy et al. into the process

disclosed by Wetesen et al. because Weseten et al. also teaches the preparation of micron and submicron particles consisting of poorly water soluble bioactive agents and their use in drug delivery systems. One skilled in the art would have been motivated to prepare pulverulent active substances by utilizing the process of both Wetesen et al. and Timothy et al. with a reasonable expectation of success.

Response to Arguments

4. Applicant's arguments filed 04/24/08 have been fully considered but they are not persuasive.

Applicant argues that "Westesen discloses an emulsion preparation with active agent rather than the instantly claimed bioactive agents being dispersed in an aqueous phase. Applicant further argues that Applicants' process additionally seeks to minimize an emulsified state of the system to a maximum extend of a few milliseconds (see paragraph [0132], last sentence) and uses a process defined by the existence of suspended particles even before passing the short emulsion step. The disclosure of Timothy does not help to overcome these general discrepancies between Westesen and Applicants' claimed process of Claims 16-36 and 40."

Applicants arguments are not persuasive since the prior art describes the process of preparing micron and submicron particles of bioactive agents. The process as depicted describes that a solid lipid or bioactive agent or a mixture of solid lipids is melted, stabilizers are added either to the lipid or bioactive agent and to the aqueous phase only depending on their physicochemical characteristics. Stabilizers may also be

added or exchanged after homogenization. Drugs or bioactive agents can be melted together with lipid. The aqueous phase is heated to the temperature of the melt before mixing and may contain for example, stabilizers, isotonicity agents, buffering substances, and /or preservatives. The molten compounds are emulsified in an aqueous phase by high pressure homogenization (abstract, column 11 and steps 1-8). Therefore, the suspension of active agent with an aqueous solution is also disclosed in the prior art in addition to forming emulsion. It should be noted that the instant claims have open ended "comprising" language which do not exclude from reading any other embodiments/limitations to the claims. The instant claims are not commensurate with the scope of the disclosure describing the process of preparing pulverulent substances, based on the process described on page 20 of the instant specification, there is a sequence of steps which need to be followed, the claims however lack the recitation of having specific sequence or order of steps to be followed during the process. The claims recite the process comprising: a, b, c, d and e, however, no specific sequence is mentioned. The scope of the prior art when taken as a whole, teaches all the steps, however in different sequence, the rejection is therefore maintained. Applicants statement that the instant "process additionally seeks to minimize an emulsified state of the system to a maximum extend of a few milliseconds (see paragraph [0132], last sentence) and uses a process defined by the existence of suspended particles even before passing the short emulsion step" is not reflected in claims, (although the claims are interpreted in light of the specification, limitations from the specification are not read

into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993), as such the rejection is maintained.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/

Examiner, Art Unit 1612

/Gollamudi S Kishore, Ph.D/

Primary Examiner, Art Unit 1612